

II. REMARKS

Claims 1 to 21 are pending.

It is stated in the Office Action that claims 1 to 9 are allowed, and that claims 11 to 13 and 15 to 19 are objected to as depending from a rejected base claim. For the reasons set forth below, it is submitted that amended claims 10 and 14 are allowable. As such, claims 11 to 13 and claims 15 to 19, which depend from claim 10 and claim 14, respectively, have not been amended, but, it is submitted, also are allowable.

A. Regarding the Amendments

A "Brief Description" of Figure 5B has been added. The Brief Description is supported by Figure 5B as originally filed, and at page 82, lines 1-6. As such, the Brief Description of Figure 5B does not introduce new matter.

Claims 10 and 14 have been amended to clarify that the claimed complementary polynucleotides are "fully complementary" to the recited nucleic acid molecules. It is submitted that the amendment merely clarifies the claimed subject matter, and does not add new matter.

Claims 20 and 21 also have been amended to clarify that a polynucleotide as recited is "fully complementary" to an oligonucleotide having the recited characteristics. In view of this amendment, reference to the length of the polynucleotide has been deleted as redundant. In addition, claims 20 and 21 have been amended to require that the claimed oligonucleotides comprise at least "fifteen contiguous nucleotides that are complementary to and hybridize specifically to an Mcl-1s/ΔTM splice junction" comprising the specified nucleotides. The amendment is supported, for example, at page 37, line 26, to page 38, line 12 (see, also, page 33, lines 24-28; and Figure 5B). As such, it is submitted that the amendments do not add new matter.

B. Rejections under 35 U.S.C. § 112

The objection to the specification and corresponding rejection of claims 20 and 21 under 35 U.S.C. § 112, first paragraph, as allegedly lacking an adequate written description, are respectfully traversed.

It is stated in the Office Action that claims 20 and 21 only require that at least ten nucleotides hybridize to residues comprising three nucleotides 5' and three nucleotides 3' of a nucleotide as specified, but does not require hybridization of the oligonucleotide as a whole to SEQ ID NO:1. The claims have been amended to more clearly indicate an oligonucleotide of the invention comprises "at least fifteen contiguous nucleotides that are complementary to and hybridize specifically to an Mcl-1s/ΔTM splice junction", which comprises, with respect to SEQ ID NO:1, the recited nucleotide and at least three nucleotides 5' and 3' to the recited nucleotide (claim 20) or the recited hexanucleotide sequence (claim 21). As such, the amended claims require that the claimed oligonucleotides comprise at least a 15 contiguous nucleotides that are complementary to an Mcl-1s/ΔTM splice junction.

It is submitted that the specification fully describes the structural features of the claimed genus of oligonucleotides, which includes sequences that include at least the hexanucleotide sequence comprising the splice junction, and, independently, 1 to 9 additional 5' and/or 3' nucleotides flanking the splice junction, provided the oligonucleotide contains at least 15 nucleotides. As such, it is submitted that the skilled artisan, viewing the subject application, would have known that the Applicants were in possession of the genus of claimed oligonucleotides.

It is also stated in the Office Action that the genus of oligonucleotides encompassed within claims 20 and 21 is not limited by any functional attributes. Applicants point out, however, that amended claims 20 and 21 specify that at least 15 contiguous nucleotides of the claimed oligonucleotides are complementary to and "hybridize specifically" to an Mcl-1s/ΔTM splice junction". As such, it is submitted that the claims specify a functional attribute of the

genus; i.e., that they hybridize specifically to a polynucleotide comprising an Mcl-1s/ΔTM splice junction.

For the reasons set forth above, it is submitted that the amended claims clearly set forth the structural requirements and provide a functional attribute of an oligonucleotide of the invention, and that the specification clearly describes the claimed oligonucleotides. Accordingly, it is submitted that one skilled in the art, viewing the specification, would have known that the Applicants were in possession of the claimed subject matter and, therefore, respectfully requested that the objection to the specification and corresponding rejection of claims 20 to 21 under 35 U.S.C. § 112, first paragraph, as lacking an adequate written description be removed.

C. Prior Art Rejections

The rejections of claim 21 under 35 U.S.C. § 102(b) as allegedly anticipated by any of Fu et al., Nishina et al., Georgopoulos, and Fioretti et al. are respectfully traversed.

The cited references describe various nucleotide sequences that include an AAGGAT sequence, which corresponds to the hexanucleotide sequence spanning an Mcl-1s/ΔTM splice junction. Applicants point out, however, that amended claim 21 further requires that an oligonucleotide of the invention comprises "at least fifteen contiguous nucleotides that are complementary to and hybridize specifically" to an Mcl-1s/ΔTM splice junction comprising the recited nucleotides. It is submitted that the nucleotide sequences in the cited references do not meet the requirements of the claim because the references do not describe oligonucleotides that contain, for example, at least fifteen contiguous nucleotides that are complementary to a nucleotide sequence comprising the Mcl-1s/ΔTM splice junction.

More specifically, claim 21 requires that an oligonucleotide hybridize specifically to operatively linked and contiguous nucleotides 2412 to 2414/3768 to 3770 as set forth in SEQ ID NO:1. The required hexanucleotide sequence is shown in bold in the sequence labeled "Mcl-1s/ΔTM splice junction", below. Since claim 21 further requires that the oligonucleotide is at least 15 nucleotides in length and complementary to the nucleotide sequence comprising

the junction (i.e., nucleotide sequences of SEQ ID NO:1), and accounting for the six recited nucleotides flanking the splice junction, an oligonucleotide of claim 21 can contain, independently, 1 to 9 nucleotides of SEQ ID NO:1 that 5' and/or 3' to the hexanucleotide sequence, provided that the total is at least 15 (e.g., the hexanucleotide + 3 nucleotides 5' +6 nucleotides 3' = 15). Accordingly, the sequence labeled "Mcl-1s/ΔTM splice junction", below, includes the 9 nucleotides of SEQ ID NO:1 that are 5' to position 2412, and the 9 nucleotides that are 3' to position 3770. Also shown are the sequences of the cited references as set forth in the Office Action, aligned with respect to the hexanucleotide sequence (bold) comprising the splice junction, and showing by underlining nucleotides of the reference sequence that also are present in the Mcl-1s/ΔTM sequence.

Mcl-1s/ΔTM splice junction -	CCGGCCTTCCAAG- GATGGGTTTGTG
Fu et al.	<u>GAAAG</u> - GATGGGTGTGTATT CAGG
Nishina et al.	<u>GTCCAAG</u> GATGGAGACCT
Georgopoulos	AGG <u>CGCCATT</u> CCAAG- GATAACACC
Fioretti et al.	ACTGAT <u>TTCTT</u> CCAAG- GATGT GGG

It is clear from the alignment that none of the reference sequences comprises 15 contiguous nucleotides that are the same as that of Mcl-1s/ΔTM sequence. At best, Fioretti et al. describe an oligonucleotide that contains 12 contiguous nucleotides that correspond to a nucleotide sequence comprising the splice junction (or a polynucleotide fully complementary thereto). However, the references do not teach or suggest oligonucleotides that comprises 15 contiguous nucleotides that are complementary to a sequence of the splice junction (or a polynucleotide fully complementary thereto) as required by claim 21. Accordingly, it is respectfully requested that the rejection of claim 21 under 35 U.S.C. § 102(b) be removed

The rejections of claim 20 under 35 U.S.C. § 102(b) as allegedly anticipated by any of LeCuyer et al., Lopez-Nieto et al., Fisher et al., Saiki et al., Ellar et al., Cech et al., Kroeger et al., and Crea et al. are respectfully traversed.

It is stated in the Office Action that the cited references describe sequences that are at least 10 nucleotides in length and would hybridize specifically to a nucleotide sequence comprising the recited nucleotide positions of SEQ ID NO:1, or a sequence complementary thereto. As discussed above, claim 20 has been amended to more clearly indicate that an oligonucleotide sequence of the invention comprises at least 15 contiguous nucleotides that are complementary to and hybridize specifically to a splice junction as specified (or a polynucleotide fully complementary thereto). A comparison of the reference sequence with the nucleotide sequence the Mcl-1s/ΔTM splice junction, as set forth above, reveals that none of the references sequences comprises at least 15 nucleotides complementary to a nucleotide sequence of an Mcl-1s/ΔTM splice junction as required by the claims. Accordingly, it is submitted that none of the references anticipates the claimed oligonucleotides and, therefore, respectfully requested that the rejection of claim 20 under 35 U.S.C. § 102(b) be removed

The rejection of claims 10 and 14 under 35 U.S.C. § 102(b) as allegedly anticipated by the New England Biolabs catalog is respectfully traversed.

It is maintained that the claims read on random hexamers as described in the Catalog because the recitation of a "polynucleotide complementary" to the recited oligonucleotide does not contain a size limitation. Claims 10 and 14 have been amended to clarify that the polynucleotide is "fully complementary" to a recited oligonucleotide, which comprises at least fifteen nucleotides. Accordingly, it is submitted that the hexamers described in the Catalog do not anticipate the claimed oligonucleotides and, therefore, respectfully requested that the rejection of claims 10 and 14 under 35 U.S.C. § 102(b) be removed.

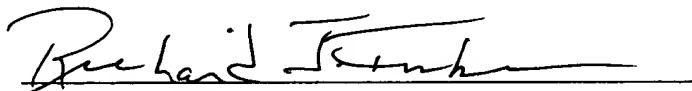
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In view of the amendments and the above remarks, it is submitted that the claims are in condition for allowance and a notice to that effect is respectfully requested. The Examiner is invited to contact Applicants' undersigned representative if there are any questions relating to this application.

No fee is deemed necessary in connection with the filing of this communication. However, if a fee is required, the Commissioner is hereby authorized to charge any required fee associated with this communication, or credit any overpayments, to Deposit Account No. 50-1355.

Respectfully submitted,


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